

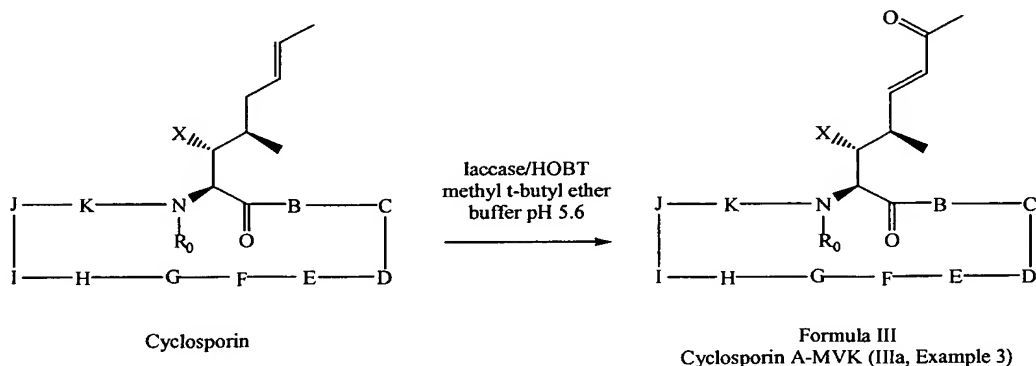
Amendments to the Specification

Please replace the section beginning at page 62, line 32 and ending at page 64, line 6 with the following amended section:

[0079] Laccase from ~~*Triametes*~~ *Trametes versicolor* in combination with mediators, such as ABTS, NHA, and HOBT, are used as bleaching agents for lignin degradation and pulp bleaching in the paper industry. In organic synthesis, laccase mediated oxidation is used for the transformation of an aromatic methyl group to an aromatic aldehyde (Fritz-Langhals et al., "Synthesis of Aromatic Aldehydes by Laccase-Mediator Assisted Oxidation," *Tetrahedron Lett.*, 39:5955-5956 (1998), which is hereby incorporated by reference in its entirety) as well as the conversion of a benzyl alcohol to benzaldehyde (Potthast et al., "A Novel Method for the Conversion of Benzyl Alcohols to Benzaldehydes by Laccase-Catalyzed Oxidation," *J. Mol. Cat., A* 108:5-9 (1996), which is hereby incorporated by reference in its entirety).

[0080] The HOBT-mediated laccase oxidation of cyclosporins is a novel application for the laccase enzyme. Treatment of cyclosporins, including cyclosporin A, with HOBT-mediated laccase oxidation conditions results in the preparation of cyclosporin methyl vinyl ketones (Cs-MVK) of Formula III. The net effect of this biocatalytic process is to convert the position one amino acid side chain terminus from the "(E)-2-butenyl" moiety to a terminal "methyl vinyl ketone," as shown in Scheme 1.

Scheme 1



The more likely products that are expected from the HOBT-mediated laccase oxidation are products of allylic oxidation of the methyl or methylene positions, i.e., primary or secondary alcohols and more highly oxidized products arising from these, i.e., aldehydes or ketones. These expected products, however, are minor reaction products at best. The formation of the Cs-MVK (Formula III) as the major product via the HOBT-mediated laccase oxidation is unexpected and unprecedented. This biocatalytic process works best using HOBT as the mediator, however the present invention includes the use of other known mediators like ABTS, VA, NHA, or other mediators known in the art. Also, the present invention includes the use of laccase enzyme from other known sources, e.g., [[*T.*]] *Trametes villosa*, [[*P.*]] *Pleurotus ostreatus*, [[*P.*]] *Polyporus versicolor*, or other known organisms from which laccase has been found.